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# Development of a general, enantioselective organocatalytic Mukaiyama–Michael reaction with α,β-unsaturated aldehydes

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ABSTRACT

LUMO-lowering organocatalysis has been extended to promote the conjugate addition of *S*-alkyl and 1-pyrrolyl silylketene acetals to α,β-unsaturated aldehydes, yielding both, *syn* and *anti* Mukaiyama–Michael products with high levels of enantioselectivity. This strategy allows for the generation of chemically useful 1,5-dicarbonyl systems and again highlights the utility of organocatalysis.



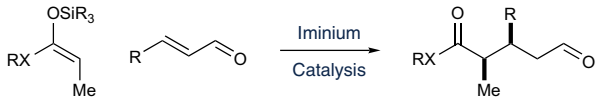
## 1. Introduction

Since its discovery in 1974, the Mukaiyama–Michael reaction has become a powerful chemical tool for carbon–carbon fragment couplings with the accompanying formation of vicinal carbon-sp$^3$ stereochemistry.[1] During this time, the inherent selectivity of latent enolates (such as silylketene acetals and enol silanes) to undergo conjugate addition to unsaturated ketones, imides and esters in the presence of Lewis acids has rendered the Mukaiyama–Michael a mainstay transformation in chemical synthesis.[2,3] It is surprising to consider, therefore, that α,β-unsaturated aldehydes have been largely bypassed as electrophilic coupling partners in this venerable 1,4-addition. This deficiency in Mukaiyama–Michael technology may arise, in part, from the documented selectivity of Lewis acids to promote 1,2-formyl activation (Eq. 1) in preference to 1,4-olefin addition (Eq. 2) with ambident electrophiles such as α,β-unsaturated aldehydes.[4,5] Herein, we reveal that iminium organocatalysis using chiral imidazolidinones has enabled the enantioselective Mukaiyama–Michael reaction of simple unsaturated aldehydes with a variety of silylketene acetals.[6] Moreover, we document that the use of silylkene acetals derived from thioesters or pyrrole amides allows selective access to *syn*- or *anti*-2,3-disubstituted, 1,5-dicarbonyl products respectively. This non-traditional approach to the Mukaiyama–Michael reaction further serves to highlight the complementary nature of LUMO-lowering iminium and metal catalysis.

**Lewis Acid Catalysis: 1,2-Addition, Mukaiyama-Aldol**


(1)

**Organocatalysis: 1,4-Addition, Mukaiyama-Michael**




(2)

## 2. Results and discussion

### 2.1. Design plan

The capacity of chiral secondary amines to catalyze the conjugate addition of a wide range of π-nucleophiles to α,β-unsaturated aldehydes has been well established.[7] We sought to extend this mechanism of action to the addition of latent enolate equivalents such as silylketene acetals, to provide acyclic Mukaiyama–Michael adducts with high levels of diastereo- and enantiocontrol. Molecular modeling of the iminium ion formed from the condensation of an α,β-unsaturated aldehyde and imidiazolidinone catalyst **1** revealed that such a substrate should be inactive towards 1,2-addition due to non-bonding interactions between the silyl enolate and the catalyst framework (MM3-**2**).[8] As such, we presumed that catalyst **1** might partition such π-nucleophiles toward

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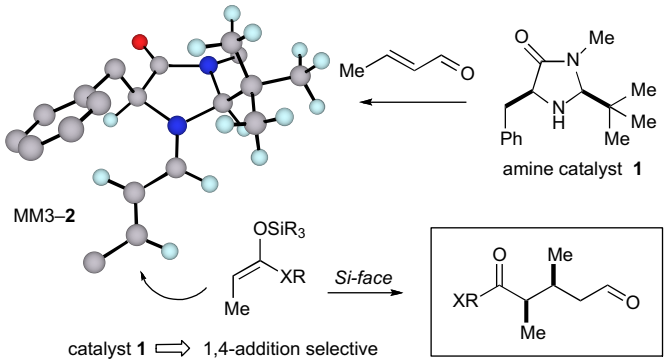
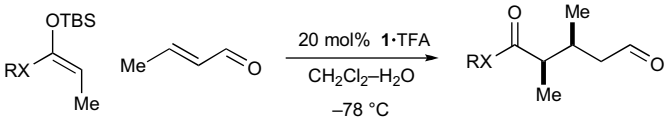
a 1,4-addition manifold while enforcing selective *Si*-face addition in the carbon–carbon bond-forming event. Moreover, we hoped that such a process might evolve to be diastereoselective (*anti* or *syn* selective) via the introduction and evaluation of various carbonyl substituents on the silyl enolate precursor.




## 2.2. Optimization studies

Our enantioselective organocatalytic Mukaiyama–Michael addition was first examined using crotonaldehyde, imidazolidinone catalyst **1** and a variety of latent enolate equivalents. As revealed in Table 1, both *O*-alkyl and *S*-phenyl substituted silylketene acetals proved to be inoperable nucleophiles due to competitive substrate hydrolysis using our standard iminium catalysis conditions (Table 1, entries 1 and 2). In contrast, *S*-alkyl (*Z*)-silyl enolates underwent rapid addition with complete 1,4-regiocontrol to furnish the desired *syn*-Mukaiyama–Michael adducts in 38–70% yield, 91% ee, and up to 5.8:1 *syn*-selectivity (Table 2, entries 3–6). Notably, the *S*-*i*-Pr substituted silylketene thioacetal exhibited the highest levels of reaction efficiency and selectivity, presumably due to its increased stability towards hydrolysis as well as amplification of the steric factors that lead to enantio- and diasterofacial control (70% conversion, 5.8:1 *syn*/*anti*, 90% ee). Unfortunately, all attempts to further expand this trend via use of the *S*-*tert*-Butyl silylketene thioacetal led only to significantly lower levels of conversion (38% conversion, 5.4:1 *syn*/*anti*, 88% ee). While the use of *Z*-enolates derived from thioesters allowed selective formation of the corresponding *syn* conjugate addition adduct, we were delighted to find that the *E*-silyl enolate of pyrrole amides led to the corresponding *anti* isomer while maintaining useful levels of enantiocontrol (entry 7, 1:17 *anti*/*syn*, 83% ee). Having established optimal conditions for the generation of both *syn*- and *anti*-Mukaiyama–Michael adducts, we next focused on defining the scope of reaction substrates for both addition protocols.

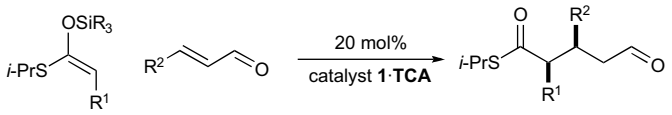
**Table 1**
Investigation of latent enolates with crotonaldehyde




| Entry | XR | % Conversion[a] | *syn*/*anti*[b] | % ee[b,c] |
|---|---|---|---|---|
| 1 | O*t*-Bu | 0 | — | — |
| 2 | SPh | 0 | — | — |
| 3 | SMe | 38 | 3.2:1 | 91 |
| 4 | SEt | 43 | 2.6:1 | 86 |
| 5 | *S*-*i*-Pr | 70 | 5.8:1 | 90 |
| 6 | *S*-*t*-Bu | 38 | 5.4:1 | 88 |
| 7 | 1-Pyrrolyl[d] | 92 | 1:17 | 83 |

[a] Product ratios determined by chiral GLC.
[b] Determined by HPLC analysis of the corresponding acyl oxazolidine.
[c] Enantiomeric excess of the major diastereomer.
[d] Performed with the (*E*)-silylketene acetal and the trichloroacetic acid salt of catalyst 1.

**Table 2**
Synthesis of *syn*-Mukaiyama–Michael adducts: scope




| Entry[a] | $SiR_3$ | $R^1$ | $R^2$ | % Yield | *syn*/*anti*[b] | % ee[c] |
|---|---|---|---|---|---|---|
| 1 | TBS | Me | Me | 76 | 10:1 | 90 |
| 2 | TBS | Me | *n*-Pr | 62 | 6:1 | 90 |
| 3 | TMS | Me | Ph | 50 | 20:1 | 90[d] |
| 4 | TBS | Me | $CO_2Me$ | 73 | 4:1 | 91 |
| 5 | TBS | Et | Me | 76 | 4:1 | 94 |
| 6 | TBS | OBn | Me | 82 | >20:1 | 90[d] |

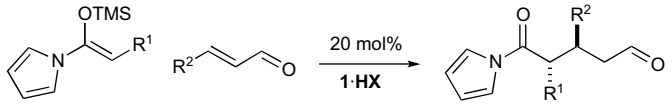
[a] Absolute and relative configuration assigned by derivitization and XRD analysis or by analogy.
[b] Determined by $^1H$ NMR analysis.
[c] Determined by HPLC analysis of the corresponding acyl oxazolidine.
[d] TFA cocatalyst.

## 2.3. Substrate scope

The scope of the *syn*-Mukaiyama–Michael reaction using *S*-*i*-Pr silylketene acetals was first explored (Table 2). As shown in Table 2, a range of electronically diverse α,β-unsaturated aldehydes readily participate in this new 1,4-conjugate addition with useful levels of diastereo- and enantioselectivity. For example, both electron-rich alkyl (entries 1 and 2, 62–76% yield, 6–10:1 *syn*/*anti*, 90% ee) and electron-withdrawing methyl ester (entry 4, 73% yield, 4:1 *syn*/*anti* 91% ee) substituents are well tolerated and give rise to highly enantioenriched products. Moreover, the use of aryl substituted enals (cinnamaldehyde) leads to highly *syn*-selective products (entry 3, 50% yield, 20:1 *syn*/*anti*, 90% ee), albeit with moderate reaction efficiency. Variation of the silylketene thioacetal is also possible (entries 5 and 6, $R^1$=Et, OBn) with the α-benzyloxy nucleophile providing the *syn* product exclusively with excellent enantiocontrol (82% yield, >20:1 *syn*/*anti*, 90% ee).

As revealed in Table 3, significant structural variation in the synthesis of *anti*-Mukaiyama–Michael products can also be accomplished using this new iminium catalysis protocol. Once again, α,β-unsaturated aldehydes that incorporate alkyl and aryl substituents readily couple with (*E*)-1-pyrrolyl silylketene acetal with good levels

**Table 3**
Synthesis of *anti*-Mukaiyama–Michael adducts: scope




| Entry[a] | $R^1$ | $R^2$ | HX | % Yield | *syn*/*anti*[b] | % ee[c] |
|---|---|---|---|---|---|---|
| 1 | Me | Me | TCA | 92 | 1:17 | 83 |
| 2 | Me | *n*-Pr | 2,4-DNBA[d] | 55 | 1:4 | 93 |
| 3 | Me | *p*-ClPh | TFA | 74 | 1:3 | 98 |
| 4 | $CH_2$cyclopentyl | Me | TBA | 68 | 1:10 | 88[e] |
| 5 | Ph | Me | TfOH | 78 | 1:3 | 87 |
| 6 | OBn | Me | TBA | 69 | 1:>20 | 93 |

[a] Absolute and relative stereochemistry assigned by chemical correlation to products of Table 3 or by analogy.
[b] Determined by $^1H$ NMR analysis.
[c] Determined by HPLC analysis of the corresponding acyl oxazolidine.
[d] 2,4-DNBA=2,4-dinitrobenzoic acid.
[e] Determined by GLC analysis.

of efficiency and stereoselectivity (entries 1–3, 55–92% yield, 1:3–17 *syn*/*anti*, 83–98% ee). Notably, this conjugate addition is successful with of a wide spectrum of substituents on the pyrrole silyl enolate component. For example, alkyl (entries 1 and 4, $R^1$=Me, $CH_2c$-pentyl), benzyloxy (entry 6, $R^1$=OBn), and aromatic substituents (entry 5, $R^1$=Ph) all maintain useful *anti*-diastereocontrol and enantioselectivities (1:3 to >20 *syn*/*anti*, 83–93% ee). It is important to note that π-nucleophiles of diverse reactivity are able to participate in this enantioselective conjugate addition without enol hydrolysis and with useful reaction efficiency if the acidity of the co-catalyst is suitably adjusted (as described in Table 3).

The various advantages of this new organocatalytic Mukaiyama–Michael reaction should be noted. For example, both *syn* and *anti* diastereomers can be readily accessed via the judicious selection of silylketene acetal architecture. Moreover, the diastereoselectivity of both the *syn* and *anti* protocols are predicted by known transition state models,[2] as is the sense of enantioinduction using the computational structure MM3-**2**. Additionally, all of the reactions described herein were performed under aerobic atmosphere with wet solvents using an inexpensive, commercial, bench stable amine catalyst.

## 3. Conclusions

In summary, LUMO-lowering organocatalysis has been extended to the development of a general Mukaiyama–Michael reaction involving *Z*- and *E*-silylketene acetals with a variety of α,β-unsaturated aldehydes. Both *syn* and *anti* 1,4-addition adducts can be obtained with good levels of enantio- and diastereocontrol through judicious selection of the π-nucleophile. Moreover, the conjugate addition product is observed as the sole regioisomer, highlighting the complementary nature of organocatalysis and metal catalysis.

## 4. Experimental section

### 4.1. General

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[9] Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32–64 mesh silica gel 63 according to the method described by Still.[10] Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization of the developed chromatogram was performed by fluorescence quenching, *p*-anisaldehyde stain, or $KMnO_4$ stain. $^1$H NMR and $^{13}$C NMR spectra were recorded on Varian Mercury-300 (300 MHz and 75 MHz, respectively) or Varian I-500 (500 MHz and 125 MHz, respectively) instruments, as noted, and are internally referenced to residual protio solvent signals. Data for $^1$H NMR are reported with chemical shift ($\delta$ ppm), multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), coupling constant (Hz), integration, and assignment. Data for $^{13}$C NMR are reported with chemical shift. IR spectra were recorded on a Perkin Elmer Paragon 1000 FTIR and are reported in terms of frequency of absorption ($cm^{-1}$). Optical rotations were recorded on a Jasco P-1010 polarimeter (WI lamp, 589 nm, 25 °C, $CHCl_3$). Mass spectra were obtained from the California Institute of Technology Mass Spectrometer Facility. Gas chromatography was performed on Agilent 5890A and Hewlett-Packard 6890 Series gas chromatographs equipped with a split/splitless capillary injection system and flame ionization detectors using the following columns: J&C industries DB-1701 (30 m×0.25 mm), Bodman Chiraldex Γ-TA (30 m×0.25 mm). HPLC analysis was performed on a Hewlett-Packard 1100 Series HPLC at 254 nm using the following Chiralcel columns: OD-H (25 cm) and OD-H guard (5 cm), AD-H (25 cm) and AD-H guard (5 cm).

### 4.2. General procedure for the organocatalytic Mukaiyama–Michael reaction

A 1-dram vial with a magnetic stirrer was charged with the appropriate (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one salt (**1**), the appropriate solvent, $H_2O$, and α,β-unsaturated aldehyde. The solution was then stirred at room temperature for 5 min before being cooled to the desired temperature. The solution was stirred for 5 min before the appropriate silylketene acetal was added. The resulting mixture was maintained at the desired temperature until consumption of the silylketene acetal as determined by TLC. The reaction was then quenched by cold filtration through silica and purified by silica gel chromatography.

### 4.3. General procedure for the preparation of acyl oxazolidinone derivatives

An analytical quantity (approximately 10 mg) of the purified Mukaiyama–Michael adduct was oxidized to the corresponding acid according to the procedure previously described in the literature.[11] The crude acid was then coupled to 2-oxazolidinone according to the procedure previously described in the literature.[3e] The resulting product was purified by silica gel chromatography (20–35% EtOAc/Hex).

### 4.4. Synthesis and characterization

#### *4.4.1. (2S,5S)-5-Benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (**1**)*

The title compound was prepared as previously described in the literature.[12] All spectral data were in agreement with those previously reported. $[\alpha]_D$ −71.8 (free base).

#### *4.4.2. tert-Butyl-1-(isopropylsulfanyl-propenyloxy)-dimethylsilane*

The title compound was prepared from thiopropionic acid *S*-isopropyl ester according to the procedure described in the literature.[3e] Bp=43 °C (160 mT); IR ($CH_2Cl_2$) 2960, 2930, 2860, 1634, 1473, 1463, 1364, 1256, 1152, 1110, 946, 853, 840, 781 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.09 (q, *J*=6.8 Hz, 1H, vinyl), 3.30 (septet, *J*=6.9 Hz, 1H, S*CH*$(CH_3)_2$), 1.68 (d, *J*=6.8 Hz, 3H, methyl), 1.26 (d, *J*=6.9 Hz, 6H, SCH(*CH*$_3)_2$), 0.93 (s, 9H, Si$(CH_3)_2$C(*CH*$_3)_3$), 0.17 (s, 6H, Si(*CH*$_3)_2$C$(CH_3)_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 145.4, 110.2, 35.0, 25.9, 25.7, 23.2, 18.1, 13.7, −4.7; HRMS (FAB peg) exact mass calcd for M+H ($C_{12}H_{27}OSiS$) requires *m*/*z* 247.1552, found *m*/*z* 247.1540.

#### *4.4.3. tert-Butyl-(1-isopropylsulfanyl-but-1-enyloxy)-dimethylsilane*

The title compound was prepared from thiobutyric acid *S*-isopropyl ester according to the procedure described in the literature.[3e] The title compound was purified by removing all volatiles from the crude product by distillation (15 mT, 100 °C bath). IR ($CH_2Cl_2$) 2960, 2931, 2896, 2860, 1627, 1472, 1463, 1363, 1256, 1151, 1130, 1112, 1063, 1006, 840, 781, 675 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.06 (t, *J*=7.5 Hz, 1H, vinyl-H), 3.30 (septet, *J*=6.6 Hz, 1H, S*CH*$(CH_3)_2$), 2.13 (app pentet, *J*=7.7 Hz, 2H, *CH*$_2$CH$_3$), 1.51 (d, *J*=6.9 Hz, 6H, SCH(*CH*$_3)_2$), 0.96–0.90 (m, 12H, SiC(*CH*$_3)_3$ and CH$_2$*CH*$_3$), 0.18 (s, 6H, Si(*t*-Bu)(*CH*$_3)_2$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 144.4, 117.9, 34.8, 25.7, 23.2, 21.9, 18.1, 14.7, −4.7; HRMS (EI) exact mass calcd for ($C_{13}H_{28}OSiS$) requires *m*/*z* 260.1630, found *m*/*z* 260.1625.

#### *4.4.4. Z-(2-Benzyloxy-1-isopropylsulfanyl-vinyloxy)-tert-butyl-dimethylsilane*

The title compound was prepared from benzyloxy-thioacetic acid *S*-isopropyl ester according to the procedure described in the literature.[3e] The title product was isolated from the crude reaction

mixture by filtration through triethylamine-treated silica (5% TEA/hexanes). IR ($CH_2Cl_2$) 2958, 2929, 2859, 1252, 1153, 839, 782 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.31–7.16 (m, 5H, ArH), 6.18 (s, 1H, vinyl-H), 4.70 (s, 2H, $CH_2Ph$), 3.19 (septet, $J$=6.6 Hz, 1H, SC*H*$(CH_3)_2$), 1.19 (d, $J$=6.6 Hz, 6H, SCH(C*H*$_3)_2$), 0.81 (s, 9H, Si(C(C*H*$_3)_3$)$(CH_3)_2$), 0.01 (s, 6H, Si(C$(CH_3)_3$)(C*H*$_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 138.2, 137.4, 133.0, 128.5, 128.0, 127.9, 74.4, 35.6, 25.9, 23.4, 18.3, −4.4; HRMS (FAB) exact mass calcd for ($C_{18}H_{30}O_2SiS$) requires $m/z$ 338.1736, found $m/z$ 338.1747.

#### 4.4.5. (2S,3R)-2,3-Dimethyl-5-oxo-pentanethioic acid S-isopropyl ester (Table 2, entry 1)

The title compound was prepared according to the general procedure from crotonaldehyde (124 μL, 1.5 mmol), *tert*-butyl-1-(isopropylsulfanyl-propenyloxy)-dimethylsilane (0.14 mL, 0.50 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TCA **1** (41 mg, 0.10 mmol) in acetone (0.25 mL) and $H_2O$ (9.0 μL, 0.50 mmol) at −78 °C for 23 h. The resulting residue was purified by silica gel chromatography (10% ether/pentane) to provide the pure product as a colorless oil in 76% yield (77 mg, 0.38 mmol). 10:1 *syn*/*anti*. *syn* Isomer: IR ($CH_2Cl_2$) 2968, 1725, 1681, 1455, 1384, 1369, 1246, 965, 752 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 9.72 (dd, $J$=2.5, 1.7 Hz, 1H, CHO), 3.62 (septet, $J$=6.9 Hz, 1H, SC*H*$(CH_3)_2$), 2.58–2.38 (m, 2H, CHOC*H*$_2$), 2.34–2.22 (m, 1H, COC*H*$(CH_3)$C), 1.32–1.24 (m, 7H, CC*H*$(CH_3)$C and SCH(C*H*$_3)_2$), 1.14 (d, $J$=6.9 Hz, 3H, COCH(C*H*$_3$)), 0.96 (d, $J$=6.6 Hz, 3H, CCH(C*H*$_3$)C); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 203.0, 201.7, 53.1, 48.8, 34.9, 31.3, 23.3, 23.2, 17.2, 14.5; HRMS (EI) exact mass calcd for M+H ($C_{10}H_{19}O_2S$) requires $m/z$ 203.1106, found $m/z$ 203.1106. $[\alpha]_D$ +34.1. Diastereomeric ratios were determined by $^1H$ NMR analysis. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone.

#### 4.4.6. (2S,3R)-2,3-Dimethyl-5-oxo-5-(2-oxo-oxazolidin-3-yl)-pentanethioic acid S-isopropyl ester

The title compound was prepared according to the general procedure. *syn* 90% ee. *syn* Isomer: IR ($CH_2Cl_2$) 2970, 1780, 1697, 1685, 1388, 1219, 965 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.04 (t, $J$=8.0 Hz, 2H, OC*H*$_2$CH$_2$N), 4.01 (t, $J$=8.2 Hz, 2H, OCH$_2$C*H*$_2$N), 3.61 (septet, $J$=6.9 Hz, 1H, SC*H*$(CH_3)_2$), 3.16–2.36 (m, 4H, COC*H*$_2$C*H*-$(CH_3)$C*H*$(CH_3)$CO), 1.29 (d, $J$=1.9 Hz, 3H, SCH(C*H*$_3$)$(CH_3)$), 1.27 (d, $J$=1.9 Hz, 3H, SCH$(CH_3)$(C*H*$_3$)), 1.12 (d, $J$=7.2 Hz, 3H, COCH(C*H*$_3$)C), 0.95 (d, $J$=6.9 Hz, 3H, COCH$_2$CH(C*H*$_3$)C); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 203.2, 172.3, 153.7, 62.2, 52.4, 42.7, 39.9, 34.7, 34.5, 32.4, 23.2, 16.2, 13.1; HRMS (FAB) exact mass calcd for ($C_{13}H_{22}NO_4S$) requires $m/z$ 288.1270, found $m/z$ 288.1264. $[\alpha]_D$ +37.1. Enantiomeric excess was determined by HPLC analysis (OD-H and OD-H guard, 3% isopropanol in hexanes, 1 mL/min); (2*R*,3*S*) isomer $t_R$=89.3 min and (2*S*,3*R*) isomer $t_R$=100.0 min.

#### 4.4.7. (2S,3R)-2-Methyl-3-(2-oxo-ethyl)hexanethioic acid S-isopropyl ester (Table 2, entry 2)

The title compound was prepared according to the general procedure from 2-hexenal (157 μL, 1.35 mmol), *tert*-butyl-1-(isopropylsulfanyl-propenyloxy)-dimethylsilane (0.13 mL, 0.45 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TCA **1** (37 mg, 0.090 mmol) in acetone (0.225 mL) and $H_2O$ (8.1 μL, 0.45 mmol) at −78 °C for 22 h. The resulting residue was purified by silica gel chromatography (3% EtOAc/Hex) to provide the pure product as a colorless oil in 62% yield (64 mg, 0.28 mmol). 6:1 *syn*/*anti*. *syn* Isomer: IR ($CH_2Cl_2$) 2961, 2931, 1725, 1680, 1463, 1367, 965 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 9.74 (t, $J$=2.0 Hz, 1H, CHO), 3.62 (septet, $J$=6.8 Hz, 1H, SC*H*$(CH_3)_2$), 2.72–2.64 (m, 1H, COC*H*$(CH_3)$C), 2.52 (ddd, $J$=17.1, 5.4, 2.0 Hz, 1H, CH*H*CHO), 2.43–2.32 (m, 2H, C*H*(*n*-Pr)C*H*HCHO), 1.43–1.22 (m, 10H), 1.14 (d, $J$=6.8 Hz, 3H, COCH(C*H*$_3$)C), 0.89 (t, $J$=6.8 Hz, 3H, CH$_2$C*H*$_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 203.0, 202.1, 51.0, 46.2, 36.1, 34.9, 33.8, 23.3, 23.1, 20.1, 14.9, 14.5; HRMS (EI) exact mass calcd for ($C_{12}H_{22}O_2S$) requires $m/z$ 230.1341, found $m/z$ 230.1341. $[\alpha]_D$ +29.5. Diastereomeric ratios were determined by $^1H$ NMR analysis. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone.

#### 4.4.8. (2S,3R)-2-Methyl-3-[2-oxo-2-(2-oxo-oxazolidin-3-yl)-ethyl]-hexanethioic acid S-isopropyl ester

The title compound was prepared according to the general procedure. *syn* 90% ee. *syn* Isomer: IR ($CH_2Cl_2$) 2962, 1782, 1697, 1684, 1387, 1223, 1197, 958 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.40 (t, $J$=7.2 Hz, 2H, OC*H*$_2$CH$_2$N), 4.02 (t, $J$=7.7 Hz, 2H, OCH$_2$C*H*$_2$N), 3.61 (septet, $J$=6.9 Hz, 1H, SC*H*$(CH_3)_2$), 3.12–2.70 (m, 3H COC*H*$_2$CH(*n*-Pr)C*H*$(CH_3)$CO), 2.52–2.40 (m, 1H, CCH(*n*-Pr)C), 1.40–1.20 (m, 10H, SCH(C*H*$_3)_2$ and C*H*$_2$C*H*$_2$CH$_3$), 1.11 (d, $J$=6.9 Hz, 3H, CH(C*H*$_3$)CO), 0.87 (t, $J$=6.6 Hz, 3H, CH$_2$C*H*$_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 203.2, 172.8, 153.7, 62.2, 50.6, 42.8, 37.1, 37.0, 34.6, 32.9, 23.3, 23.1, 20.3, 14.4, 13.1; HRMS (FAB) exact mass calcd for ($C_{15}H_{26}NO_4S$) requires $m/z$ 316.1583, found $m/z$ 316.1581. $[\alpha]_D$ +30.3. Enantiomeric excess was determined by HPLC analysis (AD-H and AD-H guard, 3% isopropanol in hexanes, 1 mL/min); (2*S*,3*R*) isomer $t_R$=25.3 min and (2*R*,3*S*) isomer $t_R$=27.0 min; *anti* diastereomers $t_R$=30.2 and 33.5 min.

#### 4.4.9. (2S,3R)-2-Methyl-5-oxo-3-phenyl-pentanethioic acid S-isopropyl ester (Table 2, entry 3)

The title compound was prepared according to the general procedure from cinnamaldehyde (76 μL, 0.60 mmol), *tert*-butyl-1-(isopropylsulfanyl-propenyloxy)-dimethylsilane (95 μL, 0.40 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TCA **1** (33 mg, 0.080 mmol) in acetone (0.20 mL), cyclohexane (14 μL), and $H_2O$ (9.0 μL, 0.50 mmol) at −78 °C for 24 h. The resulting residue was purified by silica gel chromatography (5% EtOAc/Hex) to provide the pure product as a colorless oil in 50% yield (52 mg, 0.20 mmol). 20:1 *syn*/*anti*. *syn* Isomer: IR ($CH_2Cl_2$) 2967, 1725, 1677, 1453, 963, 702 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.51 (t, $J$=2.2 Hz, 1H, CHO), 7.34–7.14 (m, 5H, ArH), 3.67 (septet, $J$=6.6 Hz, 1H, SC*H*$(CH_3)_2$), 3.44 (dt, $J$=10.4, 7.1 Hz, 1H CHPh), 2.86–2.78 (m, 1H, COC*H*$(CH_3)$C), 2.77 (dd, $J$=7.1, 1.7 Hz, 2H, CHOC*H*$_2$), 1.33 (d, $J$=6.7 Hz, 3H, SCH(C*H*$_3$)$(CH_3)$), 1.31 (d, $J$=6.0 Hz, 3H, SCH$(CH_3)$(C*H*$_3$)), 0.95 (d, $J$=6.6 Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 203.0, 200.8, 140.8, 128.9, 128.2, 127.4, 54.0, 48.3, 43.6, 35.1, 23.3, 23.2, 17.2; HRMS (EI) exact mass calcd for ($C_{15}H_{20}O_2S$) requires $m/z$ 264.1184, found $m/z$ 264.1182. $[\alpha]_D$ +49.6. Diastereomeric ratios were determined by GLC analysis (Γ-TA column, 130 °C isotherm, 1 mL/min); *syn* diastereomer $t_R$= 33.1 min and *anti* diastereomer $t_R$=36.6 min. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone.

#### 4.4.10. (2S,3R)-2-Methyl-5-oxo-5-(2-oxo-oxazolidin-3-yl)-3-phenyl-pentanethioic acid S-isopropyl ester

The title compound was prepared according to the general procedure. *syn* 90% ee. *syn* Isomer: IR ($CH_2Cl_2$) 2968, 2929, 1780, 1699, 1678, 1455, 1388, 1272, 1224, 1041, 968, 760, 702 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.32 (m, 5H, ArH), 4.35–4.15 (m, 2H, OC*H*$_2$CH$_2$N), 3.95–3.45 (m, 5H), 3.10 (app dd, $J$=16.2, 3.0 Hz, 1H, COC*H*HCH(Ph)), 2.88 (ddd, $J$=17.1, 9.9, 7.2 Hz, 1H, COCH*H*CH(Ph)), 1.33 (d, $J$=6.9 Hz, 3H, SCH(C*H*$_3$)$(CH_3)$), 1.30 (d, $J$=7.2 Hz, 3H, SCH$(CH_3)$(C*H*$_3$)), 0.93 (d, $J$=6.9 Hz, 3H, COCH(C*H*$_3$)C); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 203.0, 171.2, 153.4, 141.2, 128.4, 128.3, 126.9, 61.9, 53.3, 44.4, 42.4, 39.4, 34.7, 23.0, 22.9, 17.0; HRMS (FAB) exact mass calcd for M+H ($C_{18}H_{24}NO_4S$) requires $m/z$ 350.1426, found $m/z$ 350.1421. $[\alpha]_D$ +34.7. Enantiomeric excess was determined by HPLC analysis (OD-H and OD-H guard, 6% isopropanol in hexanes, 1 mL/min); (2*S*,3*R*) isomer $t_R$=47.6 min and (2*R*,3*S*) isomer $t_R$=54.3 min.

#### 4.4.11. (2S,3R)-5-((4S)-4-Benzyl-2-oxo-oxazolidin-3-yl)-2-methyl-5-oxo-3-phenyl-pentanethioic acid S-isopropyl ester

The title compound was prepared according to the general procedure. IR ($CH_2Cl_2$) 2971, 2928, 1782, 1702, 1674, 1454, 1388, 1355, 1213, 954, 761, 739, 702 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.26–7.03 (m, 10H, ArH), 4.38–4.26 (m, 1H, $OCH_2CH$(Bn)N), 3.95 (dd, $J$=9.0, 2.7 Hz, OC*H*HCH(Bn)N), 3.90–3.36 (m, 4H), 3.13–3.00 (m, 2H, $CH_2Ph$), 2.90–2.76 (m, 1H, COC*H*HCH(Ph)), 2.55 (dd, $J$=13.4, 9.8 Hz, 1H, COCH*H*CH(Ph)), 1.29 (d, $J$=6.9 Hz, 3H, SCH($CH_3$)($CH_3$)), 1.25 (d, $J$=6.9 Hz, 3H, SCH($CH_3$)($CH_3$)), 0.88 (d, $J$=6.9 Hz, 3H, COCH($CH_3$)C); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 203.0, 171.1, 153.3, 141.1, 135.3, 129.4, 128.9, 128.5, 128.4, 127.2, 127.0, 66.0, 55.1, 53.5, 44.7, 39.7, 37.7, 34.7, 31.2, 23.0, 22.9, 17.0; HRMS (FAB) exact mass calcd for M+H ($C_{25}H_{30}NO_4S$) requires $m/z$ 440.1896, found $m/z$ 440.1882. $[\alpha]_D$ +64.5. The title compound was recrystallized (THF/hexanes) to afford X-ray quality crystals for XRD analysis (see supplementary data).

#### 4.4.12. (2S,3R)-3-Isopropylsulfanylcarbonyl-2-(2-oxo-ethyl)-butyric acid methyl ester (Table 2, entry 4)

The title compound was prepared according to the general procedure from 4-oxo-but-2-enoic acid methyl ester (43 mg, 0.38 mmol), *tert*-butyl-1-(isopropylsulfanyl-propenyloxy)-dimethyl-silane (59 μL, 0.25 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TCA **1** (20 mg, 0.050 mmol) in acetone (0.125 mL) and $H_2O$ (4.5 μL, 0.25 mmol) at −78 °C for 22 h. The resulting residue was purified by silica gel chromatography ($CH_2Cl_2$) to provide the pure product as a colorless oil in 73% yield (45 mg, 0.18 mmol). 4:1 *syn*/*anti*. *syn* 91% ee. *syn* Isomer: $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.73 (app s, 1H, CHO), 3.71 (s, 3H, $CO_2CH_3$), 3.64 (septet, $J$=6.9 Hz, 1H, SC*H*($CH_3$)$_2$), 3.19 (qd, $J$=7.7, 3.7 Hz, 1H COC*H*($CH_3$)C), 3.01–2.87 (m, 2H, $COCH_2$C), 2.64 (td, $J$=3.2, 0.5 Hz, 1H, ($CH_2$)(CH)C*H*$CO_2CH_3$), 2.60 (d, $J$=6.9 Hz, 6H, SCH($CH_3$)$_2$), 1.20 (d, $J$=6.9 Hz, 3H, COCH($CH_3$)C); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 201.1, 199.4, 173.3, 52.1, 48.2, 43.2, 41.0, 34.9, 22.9, 22.8, 15.8; HRMS (EI) exact mass calcd for M+H ($C_{11}H_{19}O_4S$) requires $m/z$ 247.1004, found $m/z$ 247.1015. $[\alpha]_D$ +0.74. Diastereomeric ratios and enantiomeric excess were determined by GLC analysis (Γ-TA column, 130 °C isotherm, 1 mL/min); (2*S*,3*R*) isomer $t_R$=29.1 min, (2*R*,3*S*) isomer $t_R$=30.4 min, and *anti* isomer $t_R$=33.0 min.

#### 4.4.13. (2S,3R)-2-Ethyl-3-methyl-5-oxo-pentanethioic acid S-isopropyl ester (Table 2, entry 5)

The title compound was prepared according to the general procedure from crotonaldehyde (25 μL, 0.30 mmol), *tert*-butyl-(1-isopropylsulfanyl-but-1-enyloxy)-dimethyl-silane (29 μL, 0.10 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TCA **1** (8.0 mg, 0.020 mmol) in diethyl ether (0.050 mL), benzyl methyl ether (5.0 μL), and $H_2O$ (1.8 μL, 0.10 mmol) at −78 °C. The solution was stirred until the reaction was judged to be complete by GLC analysis (DB-1701 column, 70 °C, 25 °C/min gradient, 1 mL/min); benzyl methyl ether $t_R$=3.75 min, 2-ethyl-3-methyl-5-oxo-pentanethioic acid *S*-isopropyl ester $t_R$=6.40 min. A yield of 76% was determined by comparison of the peak areas of benzyl methyl ether and 2-ethyl-3-methyl-5-oxo-pentanethioic acid *S*-isopropyl ester. 4:1 *syn*/*anti*. *syn* Isomer: IR ($CH_2Cl_2$) 2968, 1727, 1678, 1461, 990, 833 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.72 (dd, $J$=2.4, 1.3 Hz, 1H, CHO), 3.66 (septet, $J$=6.9 Hz, 1H, SC*H*($CH_3$)$_2$), 2.62–2.20 (m, 3H, CHOC*H*$_2$CH($CH_3$)C*H*(Et)COS(*i*-Pr)), 1.77–1.46 (m, 3H, $CH_2CH$($CH_3$)C and $CH_2CH_3$), 1.30 (d, $J$=6.9 Hz, 6H, SCH($CH_3$)$_2$), 0.99 (d, $J$=6.1 Hz, 3H, $CH_2$CH($CH_3$)C), 0.91 (t, $J$=7.5 Hz, 3H, $CH_2CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 202.6, 201.8, 60.5, 48.3, 48.2, 34.7, 30.3, 23.0, 22.9, 17.9, 11.8; HRMS (EI) exact mass calcd for M−H ($C_{11}H_{19}O_2S$) requires $m/z$ 215.1106, found $m/z$ 215.1114. $[\alpha]_D$ +2.0. Diastereomeric ratios were determined by $^1H$ NMR analysis. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone.

#### 4.4.14. (2S,3R)-2-Ethyl-3-methyl-5-oxo-5-(2-oxo-oxazolidin-3-yl)-pentanethioic acid S-isopropyl ester

The title compound was prepared according to the general procedure. *syn* 94% ee. *syn* Isomer: IR ($CH_2Cl_2$) 2966, 1779, 1682, 1456, 1386, 1223, 1109, 1042, 990, 827, 761, 707 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.41 (t, $J$=8.2 Hz, 2H, $OCH_2CH_2N$), 4.02 (t, $J$=7.4 Hz, 2H, $OCH_2CH_2N$), 3.65 (septet, $J$=6.9 Hz, 1H, SC*H*($CH_3$)$_2$), 3.03–2.85 (m, 1H, CHCOS(*i*-Pr)), 2.53–2.36 (m, 2H, $COCH_2$), 1.80–1.40 (m, 4H), 1.29 (d, $J$=6.9 Hz, 6H, SCH($CH_3$)$_2$), 0.99 (d, $J$=6.6 Hz, 3H, CHC*H*$_3$), 0.90 (t, $J$=7.2 Hz, 3H, $CH_2CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 202.5, 172.3, 153.4, 62.0, 60.0, 42.5, 39.6, 34.6, 31.8, 26.3, 22.9, 21.8, 17.1, 12.0; HRMS (EI) exact mass calcd for M+H ($C_{14}H_{24}NO_4S$) requires $m/z$ 302.1426, found $m/z$ 302.1440. $[\alpha]_D$ +20.7. Enantiomeric excess was determined by HPLC analysis (OD-H and OD-H guard, 1% ethanol in hexanes, 1 mL/min); *syn* isomers $t_R$=54.2 and 68.4 min and *anti* isomers $t_R$=48.6 and 49.8 min.

#### 4.4.15. (2S,3R)-2-Benzyloxy-3-methyl-5-oxo-pentanethioic acid S-isopropyl ester (Table 2, entry 6)

The title compound was prepared according to the general procedure from crotonaldehyde (85 μL, 1.0 mmol), *Z*-(2-benzyloxy-1-isopropylsulfanyl-vinyloxy)-*tert*-butyl-dimethylsilane (0.12 mL, 0.34 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TFA **1** (25 mg, 0.068 mmol) in $CH_2Cl_2$ (0.17 mL) and $H_2O$ (6.1 μL, 0.34 mmol) at −78 °C for 24 h. The resulting residue was purified by silica gel chromatography (10% EtOAc/Hex) to provide the pure product as a colorless oil in 82% yield (82 mg, 0.28 mmol). >20:1 *syn*/*anti*. *syn* Isomer: IR ($CH_2Cl_2$) 2966, 1724, 1676, 1456, 1124, 1087, 1059, 738, 699 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.62 (t, $J$=2.2 Hz, 1H, CHO), 7.40–7.28 (m, 5H, ArH), 4.81 (d, $J$=11.5 Hz, 1H, PhC*H*HO), 4.35 (d, $J$=11.5 Hz, 1H, PhCH*H*O), 3.86 (d, $J$=4.4 Hz, 1H, COCH(OBn)C), 3.65, (septet, $J$=7.1 Hz, 1H, SC*H*($CH_3$)$_2$), 2.66–2.45 (m, 2H, CHOCH*HCH*($CH_3$)C), 2.31 (ddd, $J$=16.5, 6.6, 1.6 Hz, 1H, CHOC*H*HC), 1.34 (d, $J$=3.3 Hz, 3H, SCH($CH_3$)($CH_3$)), 1.32 (d, $J$=3.3 Hz, 3H, SCH($CH_3$)($CH_3$)), 0.98 (d, $J$=7.1 Hz, 3H, $CHOCH_2CH$($CH_3$)C); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 202.7, 201.2, 137.1, 128.6, 128.4, 128.2, 86.8, 73.9, 47.4, 32.3, 25.9, 23.3, 23.2, 15.0; HRMS (FAB) exact mass calcd for M+H ($C_{16}H_{23}O_3S$) requires $m/z$ 295.1368, found $m/z$ 295.1376. $[\alpha]_D$ +77.1. Diastereomeric ratios were determined by $^1H$ NMR or GLC analysis (DB-1701 column, 70 °C, 25 °C/min gradient to 280 °C isotherm, constant flow 1 mL/min); *syn* Isomer $t_R$=9.02 min and *anti* isomer $t_R$=9.38 min. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone.

#### 4.4.16. (2S,3R)-2-Benzyloxy-3-methyl-5-oxo-5-(2-oxo-oxazolidin-3-yl)-pentanthioic acid S-isopropyl ester

The title compound was prepared according to the general procedure. *syn* 90% ee. *syn* Isomer: IR ($CH_2Cl_2$) 2968, 2929, 2869, 1782, 1697, 1677, 1479, 1455, 1388, 1312, 1223, 1102, 1042, 755, 701 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.41–7.25 (m, 5H, ArH), 4.86 (d, $J$=11.5 Hz, 1H, OC*H*HCH$_2$N), 4.35 (d, $J$=8.2 Hz, 2H, $CH_2Ph$), 4.32 (d, $J$=5.0 Hz, 1H, OCH*H*CH$_2$N), 4.00 (d, $J$=3.9 Hz, 1H, COCH(OBn)C), 3.97–3.71 (m, 2H, $OCH_2CH_2N$), 3.65 (septet, $J$=7.1 Hz, 1H, SCH(Me)$_2$), 2.94 (dd, $J$=17.6, 8.2 Hz, 1H, COC*H*HC), 2.79 (dd, $J$=17.6, 5.5 Hz, 1H, COCH*H*C), 2.63–2.52 (m, 1H, CHMe), 1.34 (d, $J$=2.2 Hz, 3H, SCH($CH_3$)($CH_3$)), 1.32 (d, $J$=2.8 Hz, 3H, SCH($CH_3$)($CH_3$)), 0.98 (d, $J$=7.1 Hz, 3H, CH($CH_3$)); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 203.2, 171.8, 155.5, 137.5, 128.7, 128.5, 127.9, 85.9, 73.9, 62.1, 42.5, 38.5, 34.1, 33.4, 23.3, 23.3, 14.6; HRMS (EI) exact mass calcd for ($C_{19}H_{27}NO_5S$) requires $m/z$ 380.1532, found $m/z$ 380.1537. $[\alpha]_D$ +63.6. Enantiomeric excess was determined by HPLC analysis (AD-H and AD-H guard, 10% isopropanol in hexanes, 1 mL/min); *syn* Isomers $t_R$=25.1 and 31.9 min.

#### 4.4.17. 1-(1-Trimethylsilanyloxy-propenyl)-1H-pyrrole

The title compound was prepared as described in the literature.[13] All spectral data were in agreement with those previously reported.

*4.4.18. 1-(2-Benzyloxy-1-trimethylsilanyloxy-vinyl)-1H-pyrrole*

The title compound was prepared as described in the literature.[3e] All spectra data were in agreement with those previously reported.

*4.4.19. 3-Cyclopentyl-1-pyrrol-1-yl-propan-1-one*

The title compound was prepared from pyrrole and 3-cyclopentyl-propionyl chloride according to the procedure described in the literature.[13] Analytical data. Bp=125–130 °C (2 mm Hg); IR ($CH_2Cl_2$) 2948, 2866, 1717, 1469, 1331, 1277, 1118, 1071, 921, 740 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.32 (t, $J$=2.2 Hz, 2H, ArH), 6.28 (t, $J$=2.2 Hz, 2H, ArH), 2.82 (dd $J$=8.5, 7.4 Hz, 2H, $COCH_2$), 1.90–1.40 (m, 9H), 1.25–1.05 (m, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.8, 119.0, 113.0, 39.6, 33.9, 32.5, 32.4, 30.9, 25.6, 25.2; HRMS (EI) exact mass calcd for ($C_{12}H_{27}NO$) requires $m/z$ 191.1310, found $m/z$ 191.1310.

*4.4.20. 1-(3-Cyclopentyl-1-trimethylsilanyloxy-propenyl)-1H-pyrrole*

The title compound was prepared from 3-cyclopentyl-1-pyrrol-1-yl-propan-1-one according to the procedure described in the literature.[13] IR ($CH_2Cl_2$) 2953, 2869, 1723, 1682, 1470, 1312, 1254, 1200, 1087, 921, 847, 801, 725 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 6.98 (t, $J$=2.4 Hz, 2H, ArH), 6.17 (t, $J$=2.4 Hz, 2H, ArH), 4.71 (t, $J$=7.4 Hz, 1H, vinyl), 2.88–2.62 (m, 1H), 2.49–2.31 (m, 1H), 1.95–1.35 (m, 7H), 1.30–1.00 (m, 2H), 0.35 (s, 9H, TMS); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 120.7, 119.0, 108.8, 107.5, 40.2, 32.9, 32.7, 32.4, 25.2, 25.0, 2.1; HRMS (EI) exact mass calcd for M+H ($C_{15}H_{26}NOSi$) requires $m/z$ 264.1784, found $m/z$ 264.1772.

*4.4.21. 1-(2-Phenyl-1-trimethylsilanyloxy-vinyl)-1H-pyrrole*

The title compound was prepared as described in the literature.[3e] All spectral data were in agreement with those previously reported.

*4.4.22. (3R,4R)-Dimethyl-5-oxo-5-pyrrol-1-yl-pentanal (Table 3, entry 1)*

The title compound was prepared according to the general procedure from crotonaldehyde (124 μL, 1.5 mmol), 1-(1-trimethylsilanyloxy-propenyl)-1*H*-pyrrole (0.104 mL, 0.50 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TCA **1** (41 mg, 0.10 mmol) in toluene (1.0 mL) and $H_2O$ (9.0 μL, 0.50 mmol) at −78 °C for 21 h. The resulting residue was purified by silica gel chromatography (30% ether/pentane) to provide the pure product as an oil in 92% yield (89 mg, 0.46 mmol). 1:17 *syn*/*anti*. *anti* isomer: IR ($CH_2Cl_2$) 2971, 1717, 1468, 1369, 1272, 1104, 1074, 909, 744 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.72 (dd, $J$=2.4, 1.1 Hz, 1H, CHO), 7.30 (t, $J$=2.4 Hz, 2H, ArH), 6.29 (t, $J$=2.1 Hz, 2H, ArH), 3.13 (app pentet, $J$=6.4 Hz, 1H, COC*H*($CH_3$)C), 2.69–2.48 (m, 2H, CHOC*H*HC*H*($CH_3$)C), 2.31 (ddd, $J$=16.8, 8.2, 2.1 Hz, 1H, CHOCH*H*C), 1.23 (d, $J$=6.9 Hz, 3H, COCH($CH_3$)), 1.08 (d, $J$=6.9 Hz, 3H, CCH($CH_3$)C); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 201.3, 173.3, 119.0, 113.3, 46.7, 42.4, 30.8, 18.5, 14.1; HRMS (EI) exact mass calcd for ($C_{11}H_{15}NO_2$) requires $m/z$ 193.1103, found $m/z$ 193.1101. $[\alpha]_D$ −36.6. Diastereomeric ratios were determined by $^1H$ NMR analysis. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone.

*4.4.23. (2R,3R)-2,3-Dimethyl-5-(2-oxo-oxazolidin-3-yl)-1-pyrrol-1-yl-pentane-1,5-dione*

The title compound was prepared according to the general procedure. *anti* 83% ee. All spectral data were consistent with those reported in the literature.[3e]

*4.4.24. (3R)-3-((1R)-1-Methyl-2-oxo-2-pyrrol-1-yl-ethyl)-hexanal (Table 3, entry 2)*

The title compound was prepared according to the general procedure from 2-hexenal (157 μL, 1.35 mmol), 1-(1-trimethylsilanyloxy-propenyl)-1*H*-pyrrole (94 μL, 0.45 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·DNBA **1** (41 mg, 0.090 mmol) in DME (0.225 mL) and $H_2O$ (8.1 μL, 0.45 mmol) at −40 °C for 24 h. The resulting residue was purified by silica gel chromatography (10% EtOAc/Hex) to provide the pure product as an oil in 56% yield (55 mg, 0.25 mmol). 1:4 *syn*/*anti*. *anti* isomer: IR ($CH_2Cl_2$) 2959, 1715, 1469, 1273, 1103, 1073, 910, 744 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.81 (t, $J$=1.3 Hz, 1H, CHO), 7.46 (t, $J$=2.4 Hz, 2H, ArH), 6.31 (t, $J$=2.4 Hz, 2H, ArH), 3.33 (septet, $J$=5.3 Hz, 1H, SC*H*($CH_3$)$_2$), 2.71–2.32 (m, 4H, CHOC*H*$_2$C*H*(*n*-Pr)C*H*($CH_3$)), 1.46–1.10 (m, 7H, C*H*$_2$C*H*$_2$CH$_3$ and CHC*H*$_3$), 0.85 (t, $J$=6.9 Hz, 3H, $CH_2CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 201.8, 173.5, 119.3, 113.2, 45.8, 40.4, 35.1, 32.1, 20.1, 14.0, 13.2; HRMS (EI) exact mass calcd for ($C_{13}H_{19}NO_2$) requires $m/z$ 221.1416, found $m/z$ 221.1419. $[\alpha]_D$ +0.42. Diastereomeric ratios were determined by $^1H$ NMR analysis. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone.

*4.4.25. (2R,3R)-2-Methyl-5-(2-oxo-oxazolidin-3-yl)-3-propyl-1-pyrrol-1-yl-pentane-1,5-dione*

The title compound was prepared according to the general procedure. *anti* 93% ee. *anti* isomer: IR ($CH_2Cl_2$) 2959, 1785, 1700, 1685, 1467, 1391, 1334, 1311, 1265, 1225, 1119, 1100, 1046 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.57 (dd, $J$=2.6, 2.2 Hz, 2H, ArH), 6.30 (dd, $J$=2.6, 2.2 Hz, 2H, ArH), 4.43 (t, $J$=8.4 Hz, 2H, OC*H*$_2$CH$_2$N), 4.03 (t, $J$=8.4 Hz, 2H, OCH$_2$C*H*$_2$N), 3.43 (qd, $J$=6.6, 4.4 Hz, 1H, COC*H*(Me)C), 3.13 (dd, $J$=18.5, 9.2 Hz, 1H, COC*H*HC), 3.00 (dd, $J$=18.0, 4.4 Hz, 1H, COCH*H*C), 2.55–2.43 (m, 1H, CCCH(*n*-Pr)), 1.47–1.21 (m, 4H, C*H*$_2$C*H*$_2$CH$_3$), 1.18 (d, $J$=7.0 Hz, 3H, CHC*H*$_3$), 0.82 (t, $J$=6.6 Hz, 3H, $CH_2CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 173.7, 173.0, 153.7, 119.7, 113.2, 62.3, 42.8, 40.6, 37.0, 36.6, 31.5, 20.5, 14.2, 11.7; HRMS (FAB) exact mass calcd for ($C_{16}H_{23}N_2O_4$) requires $m/z$ 307.1658, found $m/z$ 307.1653; $[\alpha]_D$ −18.5. Enantiomeric excess was determined by HPLC analysis (AD-H and AD-H guard, 6% isopropanol in hexanes, 1 mL/min); (2*S*,3*S*) isomer $t_R$=38.6 min and (2*R*,3*R*) isomer $t_R$=41.6 min; *syn* Isomers $t_R$=29.4 and 35.4 min.

*4.4.26. 3-(4-Chlorophenyl)-propenal*

The title compound was prepared as described in the literature.[14] All spectral data were in agreement with those previously reported.

*4.4.27. (3R,4R)-3-(4-Chlorophenyl)-4-methyl-5-oxo-5-pyrrol-1-yl-pentanal (Table 3, entry 3)*

The title compound was prepared according to the general procedure from 3-(4-chlorophenyl)-propenal (117 mg, 0.70 mmol), 1-(1-trimethylsilanyloxy-propenyl)-1*H*-pyrrole (73 μL, 0.35 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TFA **1** (25 mg, 0.070 mmol) in THF (0.70 mL), cyclohexane (49 μL), and $H_2O$ (6.3 μL, 0.35 mmol) at −60 °C for 23 h. The resulting residue was purified by silica gel chromatography (20% EtOAc/Hex) to provide the pure product as an oil in 74% yield (75 mg, 0.26 mmol). 1:3 *syn*/*anti*. *anti* isomer: IR ($CH_2Cl_2$) 1718, 1492, 1468, 1411, 1368, 1325, 1298, 1271, 1111, 1092, 1074, 1014, 917, 894, 827, 745 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.57 (t, $J$=1.8 Hz, 1H, CHO), 7.36 (br s, 2H, ArH), 7.30 (d, $J$=8.5 Hz, 2H, ArH), 7.14 (d, $J$=8.5 Hz, 2H, ArH), 6.34 (t, $J$=2.1 Hz, 2H, ArH), 3.66 (td, $J$=9.1, 5.3 Hz, 1H, CHAr), 3.42–3.32 (m, 1H, CHCONR$_2$), 2.89–2.71 (m, 2H, C*H*$_2$CHO), 1.33 (d, $J$=7.0 Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 199.9, 172.9, 138.8, 133.2, 129.5, 129.0, 119.0, 113.8, 47.7, 43.3, 42.2, 16.7; HRMS (EI) exact mass calcd for ($C_{16}H_{17}NO_2Cl$) requires $m/z$ 290.0948, found $m/z$ 290.0951; $[\alpha]_D$ −28.0. Diastereomeric ratios were determined by $^1H$ NMR analysis. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone. *syn* Isomer: IR ($CH_2Cl_2$) 2976, 1720, 1710, 1492, 1467, 1409, 1366, 1323, 1275, 1094, 1074, 1014, 743 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.62 (dd, $J$=2.1, 1.2 Hz, 1H, CHO), 7.26–7.13 (m, 6H, ArH), 6.25 (t, $J$=2.4 Hz, 2H, ArH), 3.74 (ddd, $J$=9.7, 8.2,

5.0 Hz, 1H, CHAr), 3.43 (dt, *J*=15.2, 7.0 Hz, 1H, CHCONR$_2$), 2.98 (ddd, *J*=17.3, 4.7, 1.2 Hz, 1H, C*H*HCHO), 2.85 (ddd, *J*=17.3, 9.7, 2.1 Hz, 1H, CH*H*CHO), 1.33 (d, *J*=7.0 Hz, 3H, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 200.4, 172.7, 140.1, 133.3, 129.5, 129.2, 119.1, 113.8, 45.7, 43.9, 41.7, 15.6; HRMS (EI) exact mass calcd for (C$_{16}$H$_{17}$NO$_2$Cl) requires *m*/*z* 290.0948, found *m*/*z* 290.0945.

#### 4.4.28. (2R,3R)-3-(4-Chloro-phenyl)-2-methyl-5-(2-oxo-oxazolidin-3-yl)-1-pyrrol-1-yl-pentane-1,5-dione

The title compound was prepared according to the general procedure. *anti* 98% ee. *anti* isomer: IR (CH$_2$Cl$_2$) 1777, 1703, 1468, 1389, 1271, 1225, 1092, 745 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.39 (t, *J*=2.1 Hz, 2H, ArH), 7.29 (d, *J*=8.4 Hz, 2H, ArH), 7.19 (d, *J*=8.4 Hz, 2H, ArH), 6.34 (t, *J*=2.1 Hz, 2H, ArH), 4.31 (t, *J*=8.4 Hz, 2H, OC*H*$_2$CH$_2$), 3.94–3.72 (m, 3H, CH$_2$C*H*$_2$N and CHAr), 3.57–3.37 (m, 2H, COC*H*(CH$_3$)C and COC*H*HC), 3.16 (dd, *J*=17.3, 5.1 Hz, 1H, COCH*H*C), 1.06 (d, *J*=7.2 Hz, 3H, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 173.0, 170.9, 153.5, 139.3, 132.9, 129.8, 128.8, 119.1, 113.7, 62.1, 43.3, 43.0, 42.2, 39.5, 16.8; HRMS (FAB) exact mass calcd for M+H (C$_{19}$H$_{20}$N$_2$O$_4$Cl) requires *m*/*z* 375.1112, found *m*/*z* 375.1110. [$\alpha$]$_D$ −12.4. Enantiomeric excess was determined by HPLC analysis (OD-H and OD-H guard, 15% isopropanol in hexanes, 1 mL/min); (2*R*,3*R*) isomer $t_R$=30.4 min and (2*S*,2*S*) isomer $t_R$=34.7 min.

#### 4.4.29. (3R,4R)-4-Cyclopentylmethyl-3-methyl-5-oxo-5-pyrrol-1-yl-pentanal (Table 3, entry 4)

The title compound was prepared according to the general procedure from crotonaldehyde (99 μL, 1.2 mmol), 1-(3-cyclopentyl-1-trimethylsilanyloxy-propenyl)-1*H*-pyrrole (0.11 mL, 0.40 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TBA **1** (43 mg, 0.080 mmol) in CH$_2$Cl$_2$ (0.10 mL), toluene (0.10 mL), and H$_2$O (7.2 μL, 0.40 mmol) at −78 °C for 24 h. The resulting residue was purified by silica gel chromatography (10% EtOAc/Hex) to provide the pure product as a yellow oil in 68% yield (71 mg, 0.27 mmol). 1:10 *syn*/*anti*. *anti* isomer: IR (CH$_2$Cl$_2$) 2951, 1709, 1467, 1273, 1073, 744 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 9.71 (t, *J*=1.5 Hz, 1H, CHO), 7.34 (br s, 2H, ArH), 6.35–6.15 (m, 2H ArH), 3.34–2.92 (m, 1H), 2.7–1.8 (m, 3H), 1.78–1.36 (m, 9H), 1.16–0.85 (m, 5H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 201.4, 173.2, 119.1, 113.5, 47.4, 47.3, 38.2, 35.5, 33.3, 33.1, 32.3, 31.0, 25.1, 18.0; HRMS (EI) exact mass calcd for (C$_{16}$H$_{23}$NO$_2$) requires *m*/*z* 261.1729, found *m*/*z* 261.1724. [$\alpha$]$_D$ −14.8. Diastereomeric ratios were determined by $^1$H NMR analysis. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone.

#### 4.4.30. (2R,3R)-2-Cyclopentylmethyl-3-methyl-5-(2-oxo-oxazolidin-3-yl)-1-pyrrol-1-yl-pentane-1,5-dione

The title compound was prepared according to the general procedure. *anti* 88% ee. *anti* isomer: IR (CH$_2$Cl$_2$) 2950, 2868, 1780, 1703, 1467, 1388, 1270, 1222, 1112, 1073, 1041, 745 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.35 (br s, 2H, ArH), 6.30 (t, *J*=2.1 Hz, 2H, ArH), 4.39 (t, *J*=8.0 Hz, 2H, OC*H*$_2$CH$_2$N), 3.99 (t, *J*=8.2 Hz, 2H, OCH$_2$C*H*$_2$N), 3.23 (ddd, *J*=10.4, 5.9, 3.7 Hz, 1H, COC*H*(CH$_2$*c*-penyl)CH), 3.12 (dd, *J*=17.0, 5.1 Hz, 1H, COC*H*HCH(CH$_3$)C), 2.80 (dd, *J*=17.3, 8.0 Hz, 1H, COCH*H*CH(CH$_3$)C), 2.58–2.42 (m, 1H, CH$_2$C*H*(CH$_3$)C), 2.10–0.84 (m, 14H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 173.3, 172.1, 153.4, 119.2, 113.2, 62.0, 47.1, 42.5, 38.6, 38.3, 35.8, 33.3, 32.6, 32.4, 25.2, 25.1, 17.8; HRMS (EI) exact mass calcd for (C$_{19}$H$_{26}$N$_2$O$_4$) requires *m*/*z* 346.1893, found *m*/*z* 346.1894. [$\alpha$]$_D$ −8.0. Enantiomeric excess was determined by HPLC analysis (OD-H and OD-H guard, 15% ethanol in hexanes, 1 mL/min); *anti* isomers $t_R$=10.8 and 15.2 min.

#### 4.4.31. (3R,4S)-3-Methyl-5-oxo-4-phenyl-5-pyrrol-1-yl-pentanal (Table 3, entry 5)

The title compound was prepared according to the general procedure from crotonaldehyde (97 μL, 1.2 mmol), 1-(2-phenyl-1-trimethylsilanyloxy-vinyl)-1*H*-pyrrole (99 μL, 0.39 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TfOH **1** (31 mg, 0.078 mmol) in CHCl$_3$ (0.195 mL) and H$_2$O (7.0 μL, 0.39 mmol) at −65 °C for 24 h. The resulting residue was purified by silica gel chromatography (10% EtOAc/Hex) to provide the pure product as an oil in 78% yield (78 mg, 0.31 mmol). 1:3 *syn*/*anti*. *anti* isomer: IR (CH$_2$Cl$_2$) 1709, 1470, 1288, 914, 474 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 9.75 (app br s, 1H, CHO), 7.40–7.20 (m, 7H, ArH), 6.25–6.20 (m, 2H, ArH), 4.12 (d, *J*=9.3 Hz, 1H, CHPh), 3.10–2.88 (m, 1H, CH$_2$C*H*(CH$_3$)C), 2.67 (app dd *J*=16.5, 3.3 Hz, 1H, CHOC*H*HC), 2.49–2.35 (m, 1H, CHOCH*H*C), 0.85 (d, *J*=6.6 Hz, 3H, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 201.4, 201.2, 136.5, 129.2, 128.4, 128.1, 119.4, 113.5, 56.2, 49.2, 32.2, 17.9; HRMS (FAB) exact mass calcd for M+H (C$_{16}$H$_{18}$NO$_2$) requires *m*/*z* 256.1338, found *m*/*z* 256.1349. [$\alpha$]$_D$ −0.51. Diastereomeric ratios were determined by $^1$H NMR analysis. Enantiomeric excess was determined by conversion to the corresponding acyl oxazolidinone.

#### 4.4.32. (2S,3R)-3-Methyl-5-(2-oxo-oxazolidin-3-yl)-2-phenyl-1-pyrrol-1-yl-pentane-1,5-dione

The title compound was prepared according to the general procedure. *anti* 87% ee. *anti* isomer: IR (CH$_2$Cl$_2$) 1778, 1705, 1469, 1388, 1270, 1116, 750, 702 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.42–7.18 (m, 7H, ArH), 6.25–6.15 (m, 2H, ArH), 4.45–3.70 (m, 5H), 3.02–2.90 (m, 1H, COC*H*HC), 2.67 (dd, *J*=17.0, 7.5 Hz, 1H, COCH*H*C), 1.29–1.18 (m, 1H), 1.15 (d, *J*=6.6 Hz, 3H, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 172.0, 170.4, 136.8, 129.0, 128.7, 127.9, 119.3, 113.2, 62.0, 56.2, 42.4, 40.2, 33.0, 19.1; HRMS (EI) exact mass calcd for (C$_{19}$H$_{20}$N$_2$O$_4$) requires *m*/*z* 340.1423, found *m*/*z* 340.1434. [$\alpha$]$_D$ +0.76. Enantiomeric excess was determined by HPLC analysis (AD-H and AD-H guard, 10% ethanol in hexanes, 1 mL/min); *anti* isomers $t_R$=20.1 and 37.0 min and *syn* isomers $t_R$=23.2 and 28.5 min.

#### 4.4.33. (3R,4R)-4-Benzyloxy-3-methyl-5-oxo-5-pyrrol-1-yl-pentanal (Table 3, entry 6)

The title compound was prepared according to the general procedure from crotonaldehyde (87 μL, 1.05 mmol), 1-(2-benzyloxy-1-trimethylsilanyloxy-vinyl)-1*H*-pyrrole (97 μL, 0.35 mmol), and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one·TBA **1** (38 mg, 0.070 mmol) in THF (0.175 mL) and H$_2$O (6.3 μL, 0.35 mmol) at −78 °C for 22 h. The resulting residue was purified by silica gel chromatography (10% EtOAc/Hex) to provide the pure product as an oil in 69% yield (69 mg, 0.24 mmol). 1:42 *syn*/*anti*. *anti* isomer: IR (CH$_2$Cl$_2$) 1720, 1469, 1318, 1295, 1099, 1076, 745, 699 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 9.58 (t, *J*=1.6 Hz, 1H, CHO), 7.43–7.05 (m, 7H, ArH), 6.20–6.05 (m, 2H, ArH), 4.48 (d, *J*=11.4 Hz, 1H, OC*H*HPh), 4.22 (d, *J*=11.4 Hz, 1H, OCH*H*Ph), 4.05 (d, *J*=7.7 Hz, 1H, COCH(OBn)C), 2.62–2.41 (m, 2H, CHOC*H*$_2$), 2.28 (td, *J*=8.5, 1.6 Hz, 1H, CH$_2$C*H*(CH$_3$)CH), 0.85 (d, *J*=6.7 Hz, 3H, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 200.9, 169.5, 136.3, 128.5, 128.3, 128.3, 119.5, 113.5, 83.9, 72.6, 47.3, 32.3, 16.8; HRMS (EI) exact mass calcd for (C$_{17}$H$_{19}$NO$_3$) requires *m*/*z* 285.1365, found *m*/*z* 285.1358. [$\alpha$]$_D$ −39.8. Diastereomeric ratios and enantiomeric excess were determined by HPLC analysis of the corresponding acyl oxazolidinone.

#### 4.4.34. (2R,3R)-2-Benzyloxy-3-methyl-5-(2-oxo-oxazolidin-3-yl)-1-pyrrol-1-yl-pentane-1,5-dione

The title compound was prepared according to the general procedure.[12] *anti* 93% ee. All spectral data were in agreement with those previously reported.

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## Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.06.066.

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